NOTES ON A CASE OF HEMATOCHYLURIA, TOGETHER WITH SOME OBSERVATIONS ON THE MORPHOLOGY OF THE EMBRYO NEMATODE—FILARIA NOCTURNA.*†

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THE diagnosis of many cases of filariasis in which the adult parasites are inaccessible must depend upon the identification of the embryo nematodes. Most of the published pictures of *Filaria nocturna* have been drawn, apparently, from stained preparations and all the high power photomicrographs we have seen depict the parasite in a greatly degenerated condition and do not present the morphological details observed in a fresh preparation. The study of a case of hematochyluria during the past six months and the accessibility of a Zeiss photomicrographic apparatus have given us the opportunity of presenting the accompanying illustrations together with an abstract of our notes on the case.

ABSTRACT OF CLINICAL HISTORY.

On May 30, 1904, O'Saya, a Japanese girl, 22 years old, came under our observation. She came to Manila four years ago from a village near Nagasaki. The patient was emaciated, pale and weak and complained of passing bloody and milky urine and of attacks of abdominal pain referred chiefly to the right lumbar region. The abnormal urine was first noticed in August, 1903. This disappeared spontaneously in three months and she had no further trouble until the present attack. She claimed to have always drunk boiled water or tea, and she gave a history of previous good health. The patient was placed in the Manila Civil Hospital where during the evening and at night she was protected by a mosquito net.

She was passing a considerable amount of milky, peach-colored urine, sometimes quite bloody, which upon cooling contained large and small clots of reddish and yellowish jelly-like material. These fibrinous clots were sometimes passed through the urethra and occasioned some pain. In the centrifugate a number of filaria-like organisms were found but as none could be

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found in the peripheral circulation during the day or at night the patient was put on tonics and vesical irrigations of boracic acid until the end of June, when urotropin one gm. t.i.d. was given and the douches changed to bichloride of mercury 1–10,000 and morphine was given hypodermically for the pain.

At 9 P. M. July 23, filaria, resembling those occurring in the urine, were found in the blood from a finger. The patient was kept in a bed the foot of which was elevated and received just enough food, without fats, and liquid to sustain life, and a very weak solution of adrenalin chlorid was injected into the bladder and allowed to remain.

From August 1 to 15, the adrenalin was given by mouth, 10 to 15 drops of a 1–1000 solution every four hours during the daytime, 40 to 50 drops per day. On August 15 this treatment was stopped. At this time some swelling of the right thigh developed but subsided after a few days. The patient remained in the elevated bed until the middle of October.

On August 29, methylene blue, 0.12 gm. every four hours was given by mouth. This was stopped on September 4, on account of the occurrence of violent emesis.

At the suggestion of Dr. W. E. Musgrave we attempted to "sensitize" the adult parasites by the administration of quinine followed by the exposure of the body of the patient, through the lumbar region, to the X rays. She was given 80 to 90 grains of quinine sulphate during 48 hours followed by X ray exposures of five minutes, with the tube 18 inches away. Quinine having been administered daily, these exposures were performed at 2 to 3 P. M. on September 8, 10, 11, 12, 14, 16, 17, 18, and again after cinchonizing as before at 9 P. M. on September 29, and 30.*

On October 2, the skin over the chest and abdomen became reddened and hot. A chill and left pleurisy developed. Paracentesis produced about 600 c.c. straw colored fluid on October 8. Skin scarlet all over body. All this time the urine remained thick and bloody, but on October 10 became normal and has remained so. The temperature throughout, except during the attack of pleurisy, remained about normal, 97°–99.4° F. in the morning and 98°–99.4° F. in the evening.

Until the pleuritic attack the patient had gained 25 per cent in weight and general appearance, and although an evening temperature of 1°–3° F. persisted until October 22, she regained strength so rapidly that on October 29 and 30 the X ray was again applied for fifteen minutes, after quinine, with the bulb five inches away.

Although the patient has been at home and walking about for the past two months her chyluria has not returned. The living embryos still persist in her blood, and hence it is altogether likely that the treatment had no effect upon the adult parasites.

*Unfortunately we are unable to state the exact hardness of the X ray bulbs. In order to obtain a clear radiograph of the bones of the pelvis with this apparatus an exposure of 15 minutes with the bulb at a distance of five inches from the skin surface is necessary. Filarial embryos in a thin layer of blood, collected after cinchonizing, exposed to the rays for five minutes with the bulb 16 inches away are not killed but they squirm about in a very excited manner.

SPECIAL FEATURES OF THE CASE.

1. *The Urine.*—The urinalyses have yielded the usual findings in such cases, excepting our failure to extract fatty matters in appreciable quantities. The bloody, milky urine never altered its appearance on prolonged shaking with ether, even after it was made alkaline with sodium hydroxid, and the evaporation residue seemed to consist of other than fatty extractives, though in one instance a trace of fat was found by testing for glycerin. Its milky appearance may have been partly due to the considerable number of leucocytes it contained. The amount of albumin varied between 0.33 and 0.6 per cent. For example, an analysis by Mr. C. L. Bliss on August 26, gave: Quantity, 675 c.c.; sp. gr. 1026; reaction acid but turning, kept at 30°; albumin 0.33 per cent, average of five tests by Esbach's method; fat, trace, glycerin test.

2. *The Blood.*—Four days after admission a blood count gave 3,100,000 reds and 6,000 whites. The anemia almost disappeared as the general condition of the patient improved while at rest with the hips elevated. The excessive loss of blood did not continue for long and the anemia did not reach the grave character of such cases as Herrick[1] described as due to repeated losses of blood from hemorrhoids.

On July 30 the number of parasites per c.c. in the patient's peripheral circulation was calculated. In order to obtain drops of blood of known volume, the method of collecting it and estimating the number of parasites per c.c. used by Lathrop and Pratt was employed. Three equal-sized drops of blood were taken every two hours, beginning at 10 A. M. and ending at 6 A. M. on the following day. The average number of parasites present was then determined by counting the stained filaria on a mechanical stage. The chart shows the rise and fall in the number of filaria per c.c. present during the different times of the day and night.

In 1901, Calvert,[2] working in Manila on Filipino prisoners of war, found four cases of filariasis—lymphatic varices and hydro-

[1] *Jour. Amer. Med. Assn.*, Sept. 27, 1902; 39, p. 767.

[2] *Johns Hopkins Hosp. Bull.*, 1902, 13, p. 133.

cele. No description of the parasites is given, but they were of the nocturnal variety and probably the embryos of *Filaria bancrofti.* By means of extensive blood examinations of three cases he showed the presence of a decided eosinophilia, which was most marked at the time when the embryos were absent from the peripheral circulation. Trichinosis was excluded, but apparently no examination was made for uncinaria.

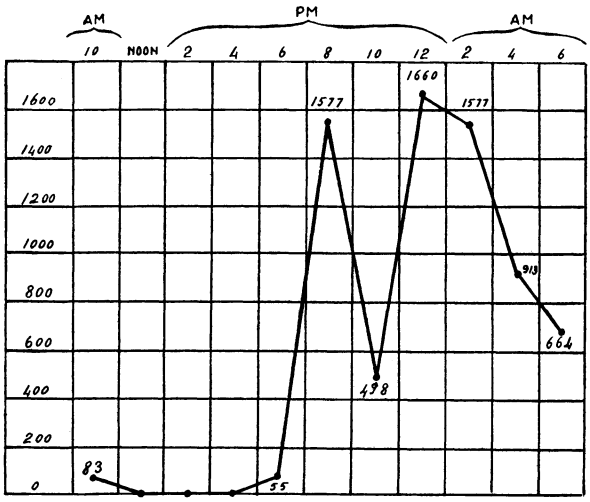

FIG. 1.—Chart showing the rise and fall in the number of filaria in the patient's peripheral circulation during different times of the day and night.

The figures in the left hand column arbitrarily represent the number of filaria per c.c. of blood, while those within the ruled squares indicate the calculated number of filaria per c.c. of blood.

In our case no such hourly counts were made. The eosinophiles varied from 6 per cent (10 A. M.) to 12 per cent (12 P. M.) and were most numerous in the peripheral circulation at the time when the embryos occurred in greatest numbers, as follows:

July 28, 10 A. M. Reds, 4,340,000; whites, 11,000.

P and T*	55%
E	6
B	4
LM	22
SM	13
	100

100 leucocytes counted; one normoblast and no filaria seen.

*P and T = Polynuclear and transitional leucocytes. E = Eosinophiles. B = Basophiles. LM = Large mononuclears. SM = Small mononuclears.

August 9, 8 P. M. Reds, 4,290,000; whites 6,000.

Differential.

8 P. M.		12 P. M.	
P and T	72.00%	P and T	71.50%
E	10.50	E	12.00
B	1.50	B	1.50
LM	2.50	LM	5.00
SM	12.50	SM	10.00
	100.00		100.00
200 leucocytes counted.		200 leucocytes counted.	

Number of Filaria per c.c.

8 P. M.	12 P. M.
489	1,079
Calculated from the average number in two slides.	Calculated from the average number in two slides.

On the morning of August 10, the patient was given an ounce of magnesium sulphate and her stool carefully examined for signs of intestinal parasites. Nothing but a few ova of *Trichocephalus dispar* was found. We believe that trichinosis can be excluded and are not aware that the eosinophilia can be influenced by the *Trichocephalus dispar* which the patient harbors.*

According to Manson[1] the presence of blood in the urine in such cases is not due to the rupture of blood vessels, but to "the formation of blood corpuscles in the lymph long retained in the varicose vessels." Our failure to alter the sanguineous character of the urine by the administration of adrenalin, locally and by the mouth, seems to support this idea. On the other hand, the development of anemia and the presence of a few normoblasts in

*REMLINGER (Constantinople) (*Compt. Rendu Soc. Biol.*, 1904, 57, p. 76) has recently noted an eosinophilia of 43 per cent in a case of multiple infection with the Medina worm. He says: "Elle est également à rapprocher de l'éosinophilia observée la *Filaria sanguinis hominis*, la *Filaria Loa*, la *Filaria Immitis*, du Chien, etc., etc."

MANSON (*Brit. Med. Jour.*, Sept. 1, 1900, 2, p. 536) has expressed the belief that a large number of filarial embryos in the peripheral circulation indicates a multiple infection with adult parasites. Apparently there is no definite information as to the fate of the embryos, but Bancroft computes their life duration at a few months. To our knowledge they have not been observed in the dead condition in the blood of man except when killed by some form of medication as in Scheube's case which was treated with picric nitrate of potash. It seems possible that they may accumulate in the blood and, if so, large numbers would merely indicate that the case was of long standing. The grade of eosinophilia together with an enumeration of the embryos by the method of Lathrop and Pratt, especially if supported by a postmortem or post operative search for the adult parasites, would throw light on this point.

[1] *Tropical Diseases*, 2d ed., 1903, p. 581.

the peripheral circulation would seem to indicate that at least a portion of the loss occurred through capillaries torn during the rupture of dilated lymph vessels, as is suggested by Scheube.[1]

3. *The embryo nematode* has been well described by Manson and our own study has been greatly influenced by his excellent descriptions. A brief description made on July 30 may be inserted here.

A fresh preparation was made at 10 P. M., ringed with vaseline and a filaria watched for some time. It underwent the usual movements of coiling, uncoiling and sliding forward and backward with its sheath. At about the junction of the middle and posterior thirds there could be seen an irregularly elongated viscus-like organ, which seemed to be composed of a granular tissue that was almost whitish by transmitted light. In about two hours the motions were reduced to very slight squirming movements. The outer contour of the filaria was clear cut, but within its lateral borders the serrated edges of the transverse fibres of the musculocutaneous layer could be traced. A little more than half-way between the anterior end and the viscus-like organ there was a refractile V-shaped papilla with its apex turned toward the lateral border of the filaria. The head end was observed with the $\frac{1}{12}$ oil im. and comp. oc. 8, and at its extreme tip a notched retractile lip could be seen. Owing to the rapidity of the retractile movements the number of notches was indistinguishable. In addition there was a short, refractile, needle-like process, which was seen to be projected and withdrawn. A few minutes later, when the movements had become slower, the lip, when retracted, showed at least three refractile teeth-like projections, and the needle-like spicule was seen to be projected at about the level of the middle tooth. (See Figs. B and C, Plate 14.)

By watching carefully the contractions and relaxations of the circular muscular fibers, three narrow, refractile, and sinuous duct-like threads could be traced backwards until they united with the anterior end of the viscus-like organ (see Fig. 2, Plate 13, and Fig. B, Plate 14). The exact manner in which they terminated

[1] *Die Krankheiten der warmen Länder*, 1904 (with complete bibliography).

anteriorly could not be made out. No particular structure could be distinguished posterior to the viscus-like organ, excepting a refractile V-shaped papilla, like the anterior one, and situated on the same side of the body at a point slightly posterior to a point half-way between the hind end of the viscus and the tip of the tail. The loose, transparent sheath could be seen projecting beyond the posterior end, but not beyond the anterior end of the parasite. In six hours ecdysis was not complete, the viscus-like organ had disappeared, and refractile granules began to make their appearance in the protoplasm. The parasite was measured just before granular degeneration set in, and was found to be: Length, 0.31 mm.; greatest breadth, 0.0075 mm.; from anterior tip to anterior end of viscus, 153 μ; length of viscus, 49.5 μ; from posterior end of viscus to tip of tail, 114.75 μ (Zeiss $\frac{1}{12}$ oc. microm. 3.) The average of four measurements is 0.327 mm. by 0.0074 mm.

We have no new morphological details to add, excepting the three duct-like threads which connect the viscus-like organ with the head end of the embryo. These must be looked for as soon as the motions of the parasite become slow enough to permit the use of an oil-immersion lens, for the granular degeneration, which sets in soon after motion ceases, obscures all finer details.

4. *Photographing the embryo.*—It is quite difficult to obtain good high-power photographs of the live filaria, and Mr. Martin's success followed only the most persistent efforts. The ray-filter must be dispensed with and the photograph taken very soon after the embryo is exposed to the rays of the electric arc, as it undergoes rapid granular degeneration and its motions cease much sooner than when subjected to ordinary daylight.

PREVALENCE OF THE DISEASE IN THE PHILIPPINE ISLANDS.

There seems to be little positive information on this point. Calvert's cases represented northern and southern Luzon. Scheube included this island, but none of the southern islands of the group, in his map showing the geographical distribution of filariasis. We have not had time to go into this side of the subject thoroughly, but inquiry shows that physicians who have been

in Manila for from 10 to 40 years have only rarely encountered cases of chyluria or chylocele. Elephantiasis seems to be absent, and filarial lymphangitis and varicose lymph glands may have been overlooked in the past. One other case of chyluria was seen in a Filipino this year by Dr. Bartels, but the patient left for the provinces before his blood could be examined. Several physicians say they have seen cases of filariasis at Iloilo.

It seems that the disease may be imported into localities where the conditions for its transmission are apparently unfavorable. Our patient has been living with four other Japanese for four, three, three, and two years respectively. An examination of these four and of a number of other Japanese living in their neighborhood was made late at night with negative results. This is rather surprising when one considers that *Culex fatigans*, the mosquito which acts as a favorable intermediate host in many parts of the world, is one of the commonest species of mosquito found in Manila. However, it should be remembered that, notwithstanding the existence of some very strong presumptive evidence, the exact manner in which filariasis is transmitted is still an open question. The brilliant observations of Manson and Bancroft, showing the metamorphosis of *Filaria nocturna* in the bodies of certain mosquitoes, and the further confirmation and extension of their views by the more recent work of Low[1] and James,[2] all tend to convince one that the disease is transmitted by the bite of certain mosquitoes.* But the facts that a number of persons can live for years with a filariated patient, when apparently a favorable intermediate host is present throughout the

[1] *Brit. Med. Jour.*, June 16, 1900, 1, p. 1456.

[2] *Ibid.*, Sept. 1, 1900, 2, p. 533.

*In the older literature on the transmission of filariasis, *culex ciliaris* was named as the intermediate host, but in recent years our knowledge of the *Culicidae* has been greatly extended, and it has been shown by Theobald (monograph "Culicidae," 1901, 2, p. 136) that *C. ciliaris* is identical with *C. pipiens*, and further that in all probability Manson's original work in China and Bancroft's later work in Australia was not done on *C. pipiens*, but on *C. fatigans* (*ibid.*, 1903, 3, p. 226). This widespread species is a voracious night feeder and occurs in large numbers in Manila. According to Low (*Brit. Med. Jour.*, June 1, 1901, 1, p. 1336), "it is the chief spreader of filarial disease in the West Indies, acting as an intermediate host for *F. nocturna*." "It is inefficicnt for *F. demarquaii*." That the intermediate host is not restricted to one genus or species of mosquito is shown by the feeding experiments of James, in which *Anopheles rosii* and possibly two species of Culex—*Culex microanulatus* and *Culex albopictus*—were shown to be suited for the metamorphosis of *Filaria nocturna*.

year, without their acquiring the disease, as in our case, and the similar cases cited by Maitland,[1] and the "relative immunity" of Europeans and others who are careful with regard to their food and drink, raise the old question whether Manson may not have been correct in his original assumption that the filaria escape from the mosquito to some watery medium and then gain entrance to their definitive host.

DESCRIPTION OF PLATES.

PLATE 13.

(Photomicrographs by Charles Martin, photographer, Bureau of Government Laboratories.)

FIG. 1.—*Filaria nocturna*, × about 390 (double exposure). Showing the general morphology and the viscus-like organ at the junction of the middle and posterior thirds of the parasite.

FIG. 2.—Head end of *Filaria nocturna*, × about 880. The sheath, the three duct-like threads connecting the anterior end of the viscus-like organ with the head end of the embryo, and the transverse striations of the musculo-cutaneous layer may be seen.

PLATE 14.

(Figures redrawn by T. Espinosa from original drawings.)

FIG. A.—Represents a dead filaria, showing granular degeneration.

FIG. B.—Drawn from a filaria just before granular degeneration set in. Proportions about correct as seen with the Zeiss $\frac{1}{12}$ oil im., comp. oc. 8. Length, 0.330 mm.; breadth, 0.00765 mm. The distance between the anatomical markings were as follows: A–B, 97.92 μ; B–C, 53.55 μ; C–D, 61.20 μ; D–E, 64.26 μ; E–F, 53.55 μ; total, 330.48 μ, or 0.33 mm.

FIG. C.—Head end of filaria, showing retracted lips and spicule.

[1] *Brit. Med. Jour.*, Sept. 1, 1900, 2, p. 537.

PLATE 13.

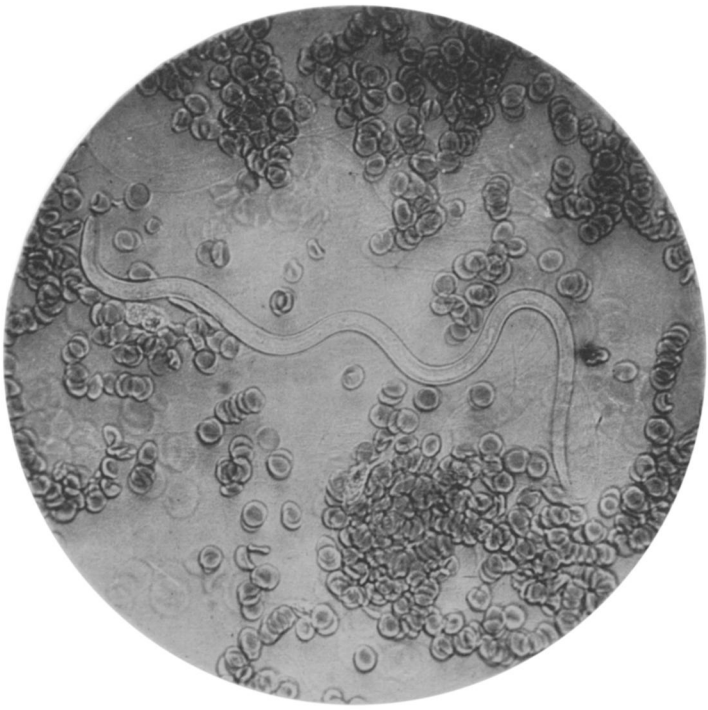

FIG. 1.

FIG. 2.

PLATE 14.